REMARKS

Claims 1-25 were pending. Applicants request that claims 2-4, 10, 11, 13, 16, 17, and 21 be cancelled without prejudice and claims 1, 5, 9, 12, 14, 15, 18-25 be amended as above. Applicants respectfully submit that the proposed amendments are adequately supported by the application as originally filed, do not raise any new issues regarding patentability and would place the application in condition for allowance. Accordingly, entry of the claim amendments and favorable reconsideration are respectfully requested.

Objections to Specification and Claims

The Abstract of the Disclosure was objected to because of the use of the term "such." The Abstract is proposed to be amended to remove this term, overcoming this objection.

Objection to claims 4 and 5 will also be overcome once the amendments above are entered, which cancels claim 4 and amends claim 5 to depend from claim 1.

Claim Rejections Under 35 U.S.C. § 112, ¶ 1

The Office Action rejected all claims under 35 U.S.C. § 112 first paragraph, for alleged lack of written description. The Office Action asserted that the specification failed to provide adequate written description for a genus of a polypeptide having a PDGF-C activities or analogs or equivalents thereof, finding applicants previous traversal arguments unpersuasive. Applicants continue to respectfully traverse this rejection, and submit that the legal analyses in both *In re Herschler* and *In re Smyth* are directly applicable even though they do not concern specifically methods using isolated nucleic acid molecules. Nevertheless, the Office Action indicated that the specification provides adequate written description for methods related to SEQ ID NOs: 1 and 2 (see page 9, last paragraph of the Office Action).

In order to expedite prosecution, and to place this case in condition for allowance, applicants have amended the claims to recite only SEQ ID NOs: 1 and 2, without acquiescing to the assertions in the final Office Action, thereby obviating the

lack of written description rejection. Applicants explicitly reserve the rights to prosecute the remainder of the subject matter not recited in the current claims in one or more divisional or continuation applications to be filed in the future.

The Office Action further rejected all claims for alleged lack of enablement, asserting that the disclosure, while enabling for the production of transgenic mice expressing SEQ ID NO: 1 or 2 (page 19, 4th to 3rd lines from the bottom), it is not enabling with regard to other transgenic non-human animals. Applicants again respectfully traverse, and submit that the references relied upon (e.g. Bishop, 1998, Mullins et al, 1996, and Wall, 1996) do not reflect the state of the art as of the filing date of the present application. In addition, the Office Action, while belaboring on the amount of experimentation necessary to produce a transgenic animal, has not shown that these experimentation is "undue" as required by the law.

Again, in order to expedite prosecution and place the present application in condition for allowance, applicants propose to amend the claims to recite only transgenic mouse in the various claims, overcoming this rejection. By making this amendment, applicants do not acquiesce to the assertions in the Office Action and reserve the right to further prosecute the claims originally presented in one or more continuation or divisional applications.

The Office Action also rejected Claim 1 for lack of enablement, asserting that the specification is enabling only as to methods wherein the cell is a pronuclei of a fertilized oocyte or an embryonic stem cell, and the method involves implanting the fertilized oocyte into a pseudopregnant mouse, or embryonic stem cell is introduced into a developing embryo, respectively.

Similarly, applicants propose to amend claim 1 and cancel claims 2 and 3 in order to expedite prosecution and place the present application in condition for allowance, without acquiescing to the assertions in the Office Action. Applicants reserve the right to further prosecute the claims originally presented in one or more continuation or divisional applications.

The Office Action rejected Claims 20-21 also for lack of enablement, asserting that the specification is only enabling to an in vitro method. Claim 21 is cancelled.

With regard to Claim 20, applicants respectfully submit that it does recite an *in vitro* method, therefore the rejection is improper and should be withdrawn. Claim 22 was similarly rejected and applicants submit that the rejection is now overcome by the amendment.

Claim Rejection Under 35 U.S.C. § 112, ¶ 2

Applicants respectfully submit that the rejections with regard to the phrase "analog having PDGF-C activity" will be overcome if the claim amendments are entered. Applicants continue to believe that using the articles "a" or "an" versus "the" in dependent claims is entirely proper, but are amending the claims to advance prosecution.

In conclusion, in view of the above amendments and remarks, applicants believe all claims are now in condition for allowance and look forward to an early indication from the Examiner to that effect. If there are any questions regarding this amendment or the application in general, a telephone call to the undersigned would be appreciated since this should expedite the prosecution of the application for all concerned.

If necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response, and please charge any deficiency in fees or credit any overpayments to Deposit Account No. 05-1323 (Docket #1064/48487).

Respectfully submitted,

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VERSION WITH MARKINGS SHOWING CHANGES MADE

IN THE CLAIMS:

Claims 2-4, 10, 11, 13, 16, 17, and 21 have been cancelled.

Claims 1, 5, 9, 12, 14, 15, 18-20, and 22-25 has been amended as follows:

1. (Twice Amended) A method for producing a transgenic[, non-human animal] mouse overexpressing a polypeptide having platelet-derived growth factor C (PDGF-C) activity or an analog or a functional fragment having a PDGF-C activity, the method comprising the steps of:

a) introducing a transgenic DNA into a mouse cell [of a non-human animal], said transgenic DNA comprising a polynucleotide sequence operably linked to a suitable promoter, said polynucleotide encoding a polypeptide comprising SEQ ID NO:1 or SEQ ID NO:2 [having PDGF-C activity, or an analog or a functional fragment having a PDGF-C activity];

[b) allowing said transgenic DNA to integrate into said cell;

c) introducing said cell from step b) into a non-human animal; and

d)]b) allowing said cell from step [c)] a) to develop into a transgenic mouse[, non-human animal],

wherein said cell of step a) is a pronuclei of a fertilized oocyte, said method further comprising implanting said fertilized oocyte into a pseudopregnant mouse; or

wherein said cell of step a) is an embryonic stem cell; said DNA is integrated into a genomic DNA of said embryonic stem cell; and said embryonic stem cell is introduced into a developing embryo.

5. (Twice Amended) The method of claim [4] 1, wherein said promoter is selected from the group consisting of alpha-myosin heavy chain promoter, keratin K14 promoter, and insulin promoter.

9. (Amended) The mouse [A transgenic, non-human animal] produced by the method of claim 1.

12. (Amended) The mouse [A transgenic, non-human animal] that is a descendant from [an animal] the mouse according to claim 9.

14. (Twice Amended) The mouse [A transgenic, non-human animal] according to Claim 9, wherein the [animal] mouse is homozygous with regard to the transgenic DNA.

15. (Amended) A cell isolated from [an animal] a mouse according to claim 9.

18. (Twice Amended) A fertilized oocyte containing transgenic DNA that encodes a polypeptide [having PDGF-C activity, or an analog or a functional fragment having a PDGF-C activity] comprising an amino acid sequence of SEQ ID NO:1 or SEQ ID NO:2.

19. (Amended) An embryonic stem cell containing transgenic DNA that encodes a polypeptide [having PDGF-C activity, or an analog or a functional fragment having a PDGF-C activity] comprising an amino acid sequence of SEQ ID NO:1 or SEQ ID NO:2.

20. (Twice Amended) A method for identifying a compound as a PDGF-C antagonist, said method comprising the steps of:

introducing said compound into a transgenic[, non-human animal] mouse overexpressing a polypeptide [having PDGF-C activity, or an analog or a functional fragment having a PDGF-C activity] comprising an amino acid sequence of SEQ ID NO:1 or SEQ ID NO:2;

monitoring in vitro a biological activity of PDGF-C in an isolated cell from said [animal] mouse; and

identifying said compound as a PDGF-C antagonist where PDGF-C biological activity is inhibited.

22. (Twice Amended) A method for identifying a compound as a PDGF-C antagonist, said method comprising the steps of:

exposing to said compound a cell isolated from a transgenic[, non-human animal] mouse overexpressing a polypeptide [having PDGF-C activity or an analog or a functional fragment thereof having a PDGF-C activity] comprising an amino acid sequence of SEQ ID NO:1 or SEQ ID NO:2;

assaying an effect of said compound on said cell in vitro; and

identifying said compound as a PDGF-C antagonist where the PDGF-C biological activity of said cell is altered.

23. (Twice Amended) A method of screening a compound for inhibition of hypertrophy, comprising the steps of:

administering a pharmaceutically active amount of said compound to a transgenic[, non-human animal] mouse overexpressing a polypeptide [having PDGF-C activity or an analog or a fragment thereof having PDGF-C activity] comprising an amino acid sequence of SEQ ID NO:1 or SEQ ID NO:2; and

monitoring cardiac development of said [animal] mouse;

determining said compound inhibits hypertrophy where said cardiac development is inhibited when compared to a control transgenic[, non-human animal] mouse in the absence of said compound.

24. (Twice Amended) A method of screening a compound for inhibition of fibrosis, comprising the steps of:

administering a pharmaceutically active amount of said compound to a transgenic[, non-human animal] mouse overexpressing a polypeptide [having PDGF-C activity or an analog or a fragment thereof having PDGF-C activity] comprising an amino acid sequence of SEQ ID NO:1 or SEQ ID NO:2; and

monitoring the cardiac development of said [animal] mouse;

determining said compound inhibits fibrosis where said cardiac development is inhibited when compared to a non-treated control transgenic[, non-human animal] mouse.

25. A transgenic[, non-human animal] mouse according to Claim 9, wherein the [animal] mouse is heterozygous with regard to the transgenic DNA encoding a polypeptide [having PDGF-C activity, or an analog or a fragment thereof having a PDGF-C activity] comprising an amino acid sequence SEQ ID NO:1 or SEQ ID NO:2.

ABSTRACT OF THE DISCLOSURE

Non-human transgenic animals overexpressing PDGF-C and cells thereof have been created. The transgenic animals contain a nucleotide sequence that encodes for platelet derived growth factor C (PDGF-C) or an analog thereof, or a functional fragment of PDGF-C or analog thereof. These animals are useful for studying disease states characterized by overexpression of PDGF-C, as well as useful for evaluating therapies intended to treat diseases characterized by overexpression of PDGF-C.